



Daniela Zimpfer

Digitally signed by
Daniela Zimpfer
DN: cn=Daniela Zimpfer,
o=European Patent
Office, ou=Legal
Services, email=d.zimpfer@epo.org
Date: 2004.09.24
10:29:56 +0200

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 1127WOORD01	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/EP 03/08677	International filing date (day/month/year) 06.08.2003	Priority date (day/month/year) 10.08.2002
International Patent Classification (IPC) or both national classification and IPC C07D401/04		E I N G A N G R E C E I V E D 30. Sep. 2004
Applicant ALTANA PHARMA AG ET AL.		Gewerblicher Rechtsschutz

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 17.02.2004	Date of completion of this report 29.09.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Kyriakakou, G Telephone No. +49 89 2399-7835 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/08677**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-37 as originally filed

Claims, Numbers

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 12 and 13 in respect of industrial applicability

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the Standard.
- ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-13
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 12 and 13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Cited Documents

WO-A-0194319 (=D1)
WO-A-9931090 (=D2)
EP-A-763534 (=D3)
Tetrahedron letters 42,8633 (=D4)
J. Med. chem. 33(6),1735 (=D5)
J. Med. chem. 44(16),2523 (=D6)
J. Med. chem. 44(16),2511 (=D7)

The indicated designation is used throughout the examination procedure

2. Novelty(Art.33(2)PCT)

The present application and the prior art documents relate to substituted pyridazinone derivatives. The main structural difference resides in the nature of the 4-substituent of the pyridazinone ring.

The subject matter of the present claims 1-13 can therefore be considered to be novel.

3. Inventive step(Art. 33(3)PCT)

3.1 The object of the present invention is to provide compounds useful as PDE4 inhibitorss.

3.2 In the light of the pharmacological tests comprised in the Description(see page 37) it is considered as credible that some of the claimed compounds have the alleged activity.

3.3 The prior art documents D1-D7 which disclose structurally similar pyridazinone derivatives having PDE4 inhibitory activity are considered to be especially relevant. With respect to the said prior art documents the main structural difference lies in the variation of the 4-substituent of the pyridazinone ring. Taking the above into account it

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is evident for the person skilled in the art that the pyridazinone group is fundamental for the PDE4 inhibitory activity and further modification of the 4-substituent results to more or less potent agents while the PDE4 inhibitory activity is maintained. The claimed compounds are therefore considered to be prima facie obvious and before an inventive step could be acknowledged, it will be necessary for the Applicant to demonstrate that the present compounds display an unexpected property or a particularly advantageous effect compared to the compounds of the closest state of the art. It has to be stressed that an inventive step could only be based on quantitative data. It should also be taken into consideration that only the structural closest prior art compounds are useful for a meaningful comparison.

An inventive step cannot therefore be acknowledged for the present claims 1-13.